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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,304	KATZ ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 11-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 11-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1103*.
4) ☒ Interview Summary (PTO-413) Paper No(s). *1103*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed October 9, 2003. Currently, claims 1-3, 11-29 are pending.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.

3. This action is FINAL.

4. Any objections and rejections not reiterated below are hereby withdrawn in view of the amendments to the claims and applicant's arguments.

Priority

5. This application claims priority to provisional application 60/222,811, filed August 4, 2000.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 11-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting loss of herterozygosity using a RPL 14 probe (SEQ ID NO: 1) as indicative of non-small cell lung cancer, does not reasonably provide enablement for detecting a loss of herterozygosity using a RPL 14 probe as indicative of any lung cancer. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method of identifying subjects at risk for the development of any cancer using an RPL14 gene probe to detect a loss of herterozygosity as indicative of any lung cancer.

The specification teaches a table which "provides an organized view of 12 patients suffering from lung cancer" (page 40, lines 8-10). It appears that the "a" sample from each patient is the non-tumorous bronchous, whereas the "b" sample from each patient is the tumorous sample. As seen in Table 1, each "a" sample had a smaller percentage of deletions (page 40, Table 1). The specification teaches "initial data shows a promising correlation between the deletion percentage and survival of a patient." The specification fails to particularly articulate what the correlation between the deletion and the survival of a patient. Moreover, it is unclear whether the increase in percentage of deletion of RPL14 gene is significantly associated with tumorous tissue or whether the showing is merely "initial data" which requires further studies and analysis. Additionally, the specification teaches that an analysis of numerous dissociated tumors with their adjacent bronchi indicated that DNA probes from 3p and 10q are associated with smoking and appear to predict for the development of non-small cell lung cancer as well as overall survival (page 42, lines 24-28). The specification also teaches that "non-smokers who develop lung cancer have much higher rates of deletions, higher even than smokers and that these results are significant ($p<0.001$)" (page 43, lines 1-2).

The art namely, Shriver et al. (Mutation Research Genomics, Vol. 406, No. 1, pages 9-23, November 1998) teaches chromosome 3p is consistently deleted in lung cancer, oral squamous cell carcinoma and renal cell carcinoma (abstract). Shriver teaches isolating a gene located at 3p21.3, namely the ribosomal protein L14 gene (RPL14)(abstract). Shriver teaches that "genotype analysis of RPL14 shows that this locus is 68% heterozygous in the normal population, compared with 25% in non-small cell lung cancer (NSCLC) cell lines ($p = 0.008$)" (abstract). Shriver teaches using FISH to identify the location of the RPL14 gene (page 12, col 2). Shriver teaches that DNA from cells and cell lines derived from six matched normal and tumor samples were analyzed (page 16, col 1). Three tumors showed loss of one RPL14 allele while the remaining three showed alterations in the length of the trinucleotide repeat (Table 3, page 16, col 1). Shriver teaches that heterozygosity of RPL14 was analyzed in squamous cell carcinoma of the head and neck (SCCHN) and the tumors exhibited normal levels of herterozygosity (page 16, col 2). Shriver teaches that the aberration of trinucleotide repeat differences was not statistically significant between lung cancer cases and race-matched controls (page 18, col 1). Shriver teaches that RPL14 is an important event in lung carcinogenesis in addition to being an informative makers for loss or alteration of the 3p21.3 critical region in cancer (page 20, col 2).

The art teaches several different types of primary lung cancer. These types include small cell lung cancer, non-small cell lung cancer and mesothelioma. As seen in Christman et al (US Pat. 5,670,314, September 23, 1997) gains and losses in chromosomes differ between non-small cell and small cell lung cancer (see Figure 3

and 4). Therefore, the analysis of one type of lung cancer is not correlative of all lung cancers.

Moreover, human ribosomal protein L14.22 gene (clone 507E08) with Genbank Accession Number AF329277 was over-expressed in gliomas. Qi (J. of Neuro-Oncology, Vol. 56, No. 3, pages 197-208, February 2000) teaches human ribosomal protein L14.22 is located on chromosome 14. Therefore, given only the arbitrary term RPL14 gene probe, it is unclear what structure is intended. The specification indicates that a RPL14 gene probe is SEQ ID NO: 1. When AF329277 and NM-003973 were blasted against each other no significant similarity was found.

Neither the specification nor the art teach the skilled artisan how to use the invention as broadly as claimed. First, the specification and the art only provide an association between non-small cell lung cancer (NSCLC) and deletion of RPL14. As seen in the art, gains and losses in chromosomes differ between non-small cell and small cell lung cancer (see Figure 3 and 4). Therefore, it is unpredictable which lung cancers are associated with deletion frequency and which cancers are not associated with the aberration. One of skill in the art would be unable to anticipate or predict which of the many cancers are associated with an aberration in hybridization of a RPL14 probe. It would require undue experimentation to analyze the broad range of cancers to determine which additional cancers, if any, are associated with the aberration. Therefore, the specification has not enabled the broad scope of the claims.

RPL14 gene probe is an arbitrary term which has been used in the art to define two different sequences. It is unclear which sequence is intended. The AF329277

Genbank Accession number has not been analyzed with respect to lung cancers. In fact, the art teaches that L14.22 is overexpressed in gliomas. Therefore, given the arbitrary term RPL14 , the skilled artisan would be unable to practice the claimed invention as a whole. The claim may be amended to recite SEQ ID NO: 1 to overcome this aspect of the instant rejection. Similarly, GC20 and PTEN/MMAC1 are arbitrary gene names. While the specification teaches GC20 is SEQ ID NO: 7, the specification does not appear to teach a sequence for PTEN/MMAC1.

With respect to GC20 gene probes and 10q22 DNA probes, and PTEN/MMAC1 gene probes, the specification does not teach the use of RPL14 in combination with each of these probes as significantly associated with lung cancer. Therefore, the skilled artisan would be required to perform additional experimentation to determine whether RPL14 in combination with each of these probes might be associated with additional types of lung cancers, the outcome of such research cannot be predicted and such further research and experimentation are both unpredictable and undue.

Response to Arguments

The response traverses the rejection. The response asserts that the information disclosure statement was filed to illustrate that the 3p21 chromosomal region is involved with a variety of cancers, not simply NSCLC. This argument has been reviewed but is not convincing because the claim is not directed to the entire 3p21 region, but specifically the RPL14 gene probe. The response admits that the evidence is "indirect with respect to evidencing the connection with RPL14, this evidence is sufficient, when taken with the information contained in the instant specification to support a broader

application of the claimed invention" (page 8). MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant." Here, the statements regarding the evidence of 3q21 involvement in all lung cancers rather than just NSCLC must be supported by evidence, not argument.

Further the references may show an "involvement" in other cancers, but the claims are specifically drawn to analyzing DNA from the test sample for LOH in RPL14 and 10q22. Moreover, several of the references are post filing date references which were not available at the time of filing. It is also noted that since Christman et al (US Pat. 5,670,314, September 23, 1997) teaches gains and losses in chromosomes differ between non-small cell and small cell lung cancer (see Figure 3 and 4), the analysis of one type of lung cancer is not correlative of all lung cancers. The claims are specifically limited to lung cancers.

It is noted that the response fails to address the arbitrary nature of the RPL14 or L14 gene name. Additionally, the response fails to address the rejection with respect to combinations of RPL14 and 10q22 not having been demonstrated to overcome the

limitations of the RPL14 probe alone. Specifically, the IDS contains several references which are involved in cancers, none of which are lung cancer.

Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

7. No claims allowable.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. After January 13, 2004, the examiner may be reached at 571-272-0743. The examiner can normally be reached Monday-Friday from 6:00 a.m. to 3:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196. After January, the receptionist may be reached at (571)272-0507

J. Goldberg

Jeanine Goldberg
Patent Examiner
January 5, 2004

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